



Effects of Albumin/Globulin Ratio on Mortality in Geriatric Patients with Hip Fracture Presenting to the Emergency Department

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Abstract

Backgrounds: Albumin and globulin are known as markers of systemic inflammation. While low albumin levels are associated with both inflammation and poor nutritional status, globulin levels may increase during inflammation. The aim of this study is to determine the prognostic value of albumin/globulin ratio on mortality after hip fractures in geriatric patients.

Methods: The data of patients aged between 65 and 111 with geriatric hip fractures who presented to the Emergency Department of Dicle University Medical Faculty Hospital between December 1, 2019, and December 31, 2021, were retrospectively analyzed. The study investigated clinical data of these patients, and the effects of the albumin/globulin ratio in biochemistry on mortality.

Results: In our study, 140 participants were included, 81 of whom were female. The average age of the participants was 79.8 ± 8.7 years. Among the participants, 73.6% had at least one comorbidity. It was found that the ages of the patients in the dying group were significantly lower compared to those in the surviving group ($p < 0.05$). Additionally, the proportion of male patients was significantly higher in the deceased group ($p < 0.05$). There was no significant difference in comorbidity rates between the dying and surviving groups ($p > 0.05$). A significant efficacy of the AGR (Albumin/Globulin Ratio) 1.12 cut-off value was observed in distinguishing between dying and surviving patients, with an area under the curve of 0.739 (0.610-0.868). The mortality rate among patients with an AGR greater than 1.12 was significantly lower ($p < 0.05$) compared to those with an AGR of 1.12 or less.

Conclusion: In conclusion, a low albumin/globulin ratio (AGR) has been associated with high mortality in geriatric patients with hip fractures.

Keywords: Albumin, Globulin, Geriatric, Hip fractures, Mortality

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Acil Servise Başvuran Kalça Kırığı Olan Geriatrik Hastalarda Albümin/Globulin Oranının Mortalite Üzerine Etkileri

Öz

Amaç: Albümin ve globülin, sistemik inflamasyonun belirteçleri olarak bilinir. Albümin düşüklüğü hem inflamasyon hem de kötü beslenme durumu ile ilişkilendirilirken, globülin düzeyleri inflamasyon sırasında artabilir. Bu çalışma, kalça kırığı olan yaşlı hastalarda, albümin/globülin oranının mortalite üzerindeki prognostik değerini belirlemeyi amaçlamaktadır.

Yöntemler: Dicle Üniversitesi Tıp Fakültesi Hastanesi Acil Servis'e 1 Aralık 2019 ile 31 Aralık 2021 tarihleri arasında başvuran 65 üstü geriatrik kalça kırığı olan hastaların verileri retrospektif olarak incelendi. Çalışmada hastaların demografik bilgileri, klinik verileri incelendi ve bu hastaların biyokimyadaki albümin/globulin oranının mortalite üzerine etkileri araştırıldı.

Bulgular: Çalışmamızda 140 hasta vardı; bunların 81'i kadın idi. Katılımcıların ortalama yaşı $79,8 \pm 8,7$ yılı. Katılımcıların %73,6'sı en az bir komorbiditeye sahipti. Ölen gruptaki hastaların yaşları, hayatta kalanlara göre anlamlı olarak düşüktü ($p < 0.05$). Erkek hasta oranı ölen grupta anlamlı olarak yüksekti ($p < 0.05$). Komorbidite oranları açısından ölen ve hayatta kalan gruplar arasında anlamlı bir fark bulunmadı ($p > 0.05$). Ölen ve yaşayan hastaların ayırımında AGR 1.12 cut off değerinin anlamlı [Eğri altı alan 0.739 (0.610-0.868)] etkinliği gözlenmiştir. AGR > 1.12 olan grupta ölen hastaların oranı AGR ≤ 1.12 olan gruptan anlamlı ($p < 0.05$) derecede daha düşüktü.

Sonuç: Sonuç olarak, AGR'nin düşük olması, kalça kırığı olan geriatrik hastalarda yüksek mortalite ile ilişkilendirilmiştir.

Anahtar kelimeler: Albümin, Globülin, Yaşlı, Kalça kırıkları, Acil Servis.

INTRODUCTION

Serum albumin and globulin are markers reflecting the systemic inflammatory process^{1,2}. As albumin can be influenced by various non-inflammatory causes, the albumin/globulin ratio (AGR) has been shown to be more successful in reflecting inflammation. With the increasing life expectancy, the incidence of conditions such as proximal femur fractures, commonly seen in advanced ages, is also rising³. Hip fractures are among the distinctive injuries in the elderly population and are one of the leading causes of death in older individuals⁴. Research indicates that about 20% of women and 30% of men die within a year after sustaining a hip fracture. A negative acute phase reactant, low levels of albumin have been found to be associated with systemic inflammation^{5,6}. However, albumin can also be affected by nutritional states, and a low albumin level can be associated with impaired nutritional conditions. Another serum protein, globulin, is closely related to the cellular and humoral immune system and generally shows polyclonal increases in systemic inflammatory conditions⁷. Due to albumin also being affected by non-inflammatory factors, the AGR has been

considered to more accurately reflect inflammatory conditions⁸. We could not find any studies in the literature investigating the effects of AGR on geriatric patients with hip fractures. Our study aims to investigate the effects of the albumin/globulin ratio on mortality in geriatric patients with hip fractures presenting to the emergency department.

METHODS

Study design

The data of 162 patients over 65 years old with geriatric hip fractures who applied to the Emergency Department of Dicle University Faculty of Medicine Hospital between December 1, 2019, and December 31, 2021, were retrospectively analyzed. Data from 22 patients were omitted from the study, because their records were incomplete. The data of 140 accessible patients, were evaluated in conjunction with Orthopedic Specialists. The study investigated clinical data of the patients, and the effects of the albumin/globulin ratio in biochemistry on mortality were examined.

The Non-Interventional Clinical Research Ethics Committee at Dicle University Faculty of Medicine approved the study and exempted it

from the requirement of informed consent (Approval No: 203, Date: May 12th, 2022). This manuscript adheres to the principles outlined in the Declaration of Helsinki (2013).

Statistical Methods

Statistical analysis was used SPSS version 24 (SPSS Inc., Chicago, Illinois) software. Normality of variables was checked using visual and analytical methods (Kolmogorov-Smirnov tests). Descriptive statistics were presented as the median for variables that were not normally distributed and as the mean for those that were normally distributed. Relationships between variables, if at least one was non-normally distributed or ordinal, were assessed using Spearman's Rank Correlation or Pearson's Correlation Coefficient. For comparing quantitative variables between two groups, either the Mann-Whitney U test or Student's T-test was applied. The Chi-square test compared categorical variables, with statistical significance set at $\alpha < 0.05$. The effect size and threshold were examined through the ROC curve analysis.

RESULTS

Our study included 140 participants, with 81 women (57.9%). The average age of the participants was 79.8 ± 8.7 years in Table I.

Table I: Age distribution and gender breakdown

	Min- Max	Median	Mean. \pm sd/n-%
Age	65.0	- 111.0 80.5	79.8 \pm 8.7
Gender	Male		59 42.1%
	Female		81 57.9%

The average age of dying group was 76.2 ± 6.2 years, with a median age of 76.0 ($p=0.045$). Among the dying group, 63.2% were male ($n=12$) ($p=0.046$). In the dying group, the patients' ages were significantly lower ($p < 0.05$) compared to those who survived. The proportion of male patients in the dying group was significantly higher ($p < 0.05$) than in the survivors. No significant difference ($p > 0.05$) was found between the dying and surviving groups in terms of comorbidity rates. Conditions such as hypertension (HT), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), goiter, chronic kidney disease (CKD), previous femur fractures, Parkinson's disease, and previous stroke (CVA) did not differ significantly ($p > 0.05$) between the died and surviving groups. The rates of dementia and epilepsy were significantly higher ($p < 0.05$) in the dying group. The surgery rates between the dying and surviving groups showed no significant difference ($p > 0.05$). The malignancy rate was significantly higher ($p < 0.05$) in the dying group. Albumin levels and AGR were significantly lower ($p < 0.05$) in the dying group, while globulin levels were significantly higher ($p < 0.05$). No significant differences ($p > 0.05$) were observed between the dying and surviving groups regarding hemoglobin, neutrophil, lymphocyte, and platelet (PLT) values. The hospital stay duration was significantly longer ($p < 0.05$) in the dying group in Table II.

Table II: Comparative analysis of clinical characteristics and outcomes between surviving and dying hospitalized patients

	Survivor		Dying		p
	Mean.±sd/n-%	Median	Mean.±sd/n-%	Median	
Age	80.3 ± 8.9	81.0	76.2 ± 6.2	76.0	0.045 ^m
Gender	Male	47 38.8%	12 63.2%		0.046 ^{x²}
	Female.	74 61.2%	7 36.8%		
Comorbidity.	(-)	31 25.6%	6 31.6%		0.584 ^{x²}
	(+)	90 74.4%	13 68.4%		
HT	62	51.2%	8	42.1%	0.459 ^{x²}
DM	39	32.2%	4	21.1%	0.326 ^{x²}
COPD	9	7.4%	2	10.5%	0.645 ^{x²}
Heart Failure	12	9.9%	5	26.3%	0.042 ^{x²}
CAD	32	26.4%	2	10.5%	0.132 ^{x²}
Goiter	4	3.3%	0	0.0%	1.000 ^{x²}
Epilepsy	0	0.0%	2	10.5%	0.018 ^{x²}
CKD	11	9.1%	3	15.8%	0.406 ^{x²}
Previous femur fractures	1	0.8%	0	0.0%	1.000 ^{x²}
Parkinson's disease	5	4.1%	2	10.5%	0.242 ^{x²}
Operation	(-)	12 9.9%	3 15.8%		0.442 ^{x²}
	(+)	109 90.1%	16 84.2%		
Malignancy	(-)	121 100.0%	14 73.7%		<0.001 ^{x²}
	(+)	0 0.0%	5 26.3%		
Albumin	3.70 ± 0.40	3.74	3.34 ± 0.50	3.34	0.002 ^m
Globulin	2.99 ± 0.39	2.97	3.42 ± 0.72	3.29	0.007 ^m
Albumin/Globulin	1.25 ± 0.19	1.24	1.02 ± 0.25	1.05	<0.001 ^t
Hemoglobin	11.8 ± 2.2	11.8	10.9 ± 2.2	11.1	0.086 ^t
Neutrophil	8.7 ± 3.8	8.2	9.9 ± 5.5	9.1	0.639 ^m
Lymphocyte	4.2 ± 25.0	1.1	1.1 ± 0.7	1.0	0.288 ^m
Duration of Hospital Stay (Days)	5.9 ± 4.7	5.0	14.2 ± 15.4	9.0	<0.001 ^m

HT: Hypertension. DM: Diabetes Mellitus. CAD: Coronary Artery Disease. CKD: Chronic Kidney Disease. m: Mann-Whitney U test. t: Student's T-test. X²: Chi-square test.

The discriminative power of the AGR was significant [area under the curve (AUC) 0.769 (0.651-0.886)] in distinguishing between dying and surviving patients. The effectiveness of a cut-off value of AGR 1.12 was significant [AUC 0.739 (0.610-0.868)] in Table III. As shown in Figure I, At the AGR 1.12 cut-off value, the sensitivity was 68.4%, positive predictive value was 34.2%, specificity was 79.3%, and negative predictive value was 94.1%.

Table III: Diagnostic performance of Albumin-Globulin Ratio (AGR) in predicting outcomes

		Area under the curve		95% Confidence Interval		p
AGR (Albumin-Globonin Ratio)		0.769		0.651 - 0.886		<0.001
AGR 1.12 Cut off		0.739		0.610 - 0.868		0.001
AGR	≤ 1.12	Survivor	Dying	Sensitivity	%	
	> 1.12	25	13			
				Positive Prediction Rate	68.4%	
				Specificity	34.2%	
				Negative Prediction Rate	79.3%	
					94.1%	

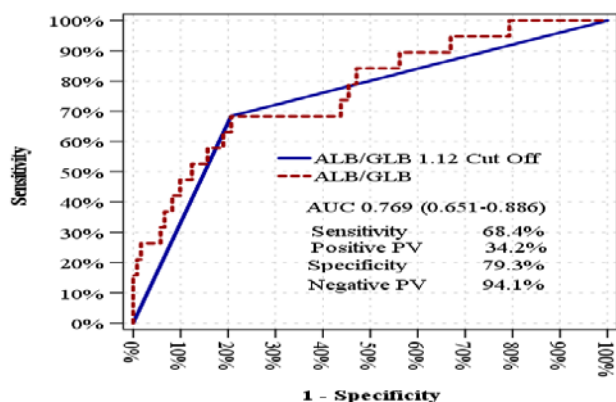


Figure 1. Albumin to globulin ratio – Sensitivity/Specificity

No significant differences ($p>0.05$) were found in age or gender distribution between groups with $AGR\leq 1.12$ and $AGR>1.12$. Comorbidity rates also showed no significant difference ($p>0.05$) between these groups. The prevalence of HT, DM, COPD, CAD, goiter, epilepsy, CKD, previous femur

fractures, and Parkinson's disease did not significantly differ ($p>0.05$) between the $AGR\leq 1.12$ and $AGR>1.12$ groups. The dementia rate was significantly lower ($p<0.05$) in the group with $AGR>1.12$ compared to the group with $AGR\leq 1.12$. No significant difference ($p>0.05$) was observed in surgery rates between the groups. The malignancy rate was significantly lower ($p<0.05$) in the $AGR>1.12$ group. Albumin and hemoglobin levels were significantly higher ($p<0.05$) in the $AGR>1.12$ group, while globulin levels were significantly lower ($p<0.05$). No significant differences ($p>0.05$) were found in neutrophil, lymphocyte, and PLT values between the $AGR\leq 1.12$ and $AGR>1.12$ groups. Hospital stay duration also showed no significant difference ($p>0.05$) between these groups. The proportion of dying patients was significantly lower ($p<0.05$) in the $AGR>1.12$ group in Table IV.

Table IV: Comparison of clinical characteristics and outcomes based on Albumin to Globulin Ratio in hospitalized patients

	AGR ≤ 1.12		AGR > 1.12		p
	Mean. \pm sd/n-%	Median	Mean. \pm sd/n-%	Median	
Age	78.2 \pm 7.7	80.0	80.3 \pm 9.0	81.0	0.172 ^m
Gender	Male	15 39.5%	44 43.1%		0.696 ^x
	Female	23 60.5%	58 56.9%		
Comorbidity	(-)	10 26.3%	27 26.5%		0.985 ^x
	(+)	28 73.7%	75 73.5%		
HT	20	52.6%	50	49.0%	0.704 ^x
DM	10	26.3%	33	32.4%	0.491 ^x
COPD	5	13.2%	6	5.9%	0.155 ^x
Heart Failure	8	21.1%	9	8.8%	0.049 ^x
CAD	7	18.4%	27	26.5%	0.323 ^x
Goiter	0	0.0%	4	3.9%	0.574 ^x
Epilepsy	2	5.3%	0	0.0%	0.072 ^x
CKD	4	10.5%	10	9.8%	0.899 ^x
Previous femur fractures	0	0.0%	1	1.0%	1.000 ^x
Parkinson's disease	3	7.9%	4	3.9%	0.389 ^x
Operation	(-)	6 15.8%	9 8.8%		0.236 ^x
	(+)	32 84.2%	93 91.2%		
Malignancy	(-)	34 89.5%	101 99.0%		0.019 ^x
	(+)	4 10.5%	1 1.0%		
Albumin	3.3 \pm 0.5	3.3	3.8 \pm 0.3	3.8	<0.001 ^t
Globulin	3.4 \pm 0.6	3.4	2.9 \pm 0.3	2.9	<0.001 ^m
Hemoglobin	10.9 \pm 2.0	10.9	12.0 \pm 2.2	12.0	0.008 ^t
Neutrophil	9.2 \pm 4.7	8.4	8.8 \pm 3.8	8.2	0.859 ^m
Lymphocyte	8.1 \pm 43.5	1.0	2.1 \pm 6.5	1.1	0.119 ^m
Duration of Hospital Stay (Days)	7.9 \pm 6.3	7.0	6.7 \pm 8.1	5.0	0.203 ^m
Dying	(-)	25 65.8%	96 94.1%		<0.001 ^x
	(+)	13 34.2%	6 5.9%		

AGR: Albumin to Globulin Ratio. HT: Hypertension. DM: Diabetes Mellitus. CAD: Coronary Artery Disease. CKD: Chronic Kidney Disease.

DISCUSSION

Hip fractures in the geriatric population present a serious health issue and are often associated with high mortality rates. Approximately 70% of hip fractures in individuals over the age of sixty occur due to low-energy trauma⁹. A meta-analysis has shown that mortality rates are highest within the first three months following a hip fracture, with men particularly at a higher risk of death¹⁰. Consistently, our study also found a significantly higher proportion of male patients in the dying group compared to survivors ($p < 0.05$). The in-hospital mortality rate is reported to be between 4% and 12%^{11,12}. Although many factors that may increase the risk of death have been identified, there is no complete consensus yet¹³.

In our study, no significant difference ($p > 0.05$) was found in the rate of comorbidities between the dying and surviving groups. Discussing the effects of the AGR on mortality after hip fractures in geriatric patients, it is important to note that AGR is an indicator of inflammation and immunity and holds prognostic significance in many diseases ($p < 0.05$). While there are no specific studies on the effects of AGR on mortality in elderly patients with hip fractures, AGR has been used as a prognostic factor in similar surgical interventions and conditions of malignancy¹⁴. Particularly, a study on patients with small-cell lung cancer (SCLC) has shown that AGR significantly impacts progression-free and overall survival². Additionally, AGR has been identified as a significant marker for the development of postoperative pancreatic fistula (POPF) in patients undergoing pancreaticoduodenectomy, with low AGR being an independent risk factor for POPF development¹⁴. This suggests that AGR can be used to predict surgical complications as well as general severe health conditions.

Our study detected significant differences in albumin and globulin levels between dying and

surviving patients. Dying patients had significantly lower AGRs, suggesting that low albumin levels may not only indicate nutritional disorders but also systemic inflammation. Low albumin levels can indicate poor overall health and increased inflammatory activity. On the other hand, higher globulin levels in dying patients support the presence of systemic inflammation. When geriatric patients with hip fractures present to the emergency department, a low AGR could be considered an indicator of possible effects on mortality, reflecting general health status and inflammation. It has been suggested that evaluating AGR alongside other biochemical parameters like RDW, albumin, and lactate might aid in increasing early intervention opportunities¹⁵.

In this research, it was found that patients with an AGR below 1.12 experienced significantly higher mortality rates compared to those with an AGR above this threshold. An AGR below 1.12 has emerged as a strong marker indicating an increased risk of death. As shown in Figure I, particularly, patients with low AGRs having higher rates of malignancy and longer hospital stays highlight the importance of this ratio in clinical practice. Moreover, the fact that patients with low AGR did not show significant differences in other comorbidities underlines the utility of this criterion as a specific mortality indicator. This implies that AGR could serve as an independent prognostic marker for predicting survival outcomes in elderly patients with hip fractures.

LIMITATIONS

This study's limitation includes not comprehensively examining other potential biochemical markers that could affect mortality besides AGR. Future studies could benefit from incorporating serial measurements of AGR and other relevant biochemical markers to better understand their temporal changes and predictive value.

CONCLUSION

In conclusion, a low AGR has been associated with high mortality in geriatric patients with hip fractures, suggesting that the routine use of AGR as a clinical biomarker could be valuable for enhancing early intervention and management strategies in this patient group. This finding underlines the importance of incorporating AGR into the routine assessment of elderly patients presenting with hip fractures, potentially aiding in the identification of those at higher risk of adverse outcomes, thus allowing for tailored, proactive medical care.

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